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| APPLICATION NO. | FILING DATE | FIRST NAMED INVENTOR | ATTORNEY DOCKET NO. | CONFIRMATION NO. |
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| 10/070,587 | 07/10/2002 | Leszek Wojnowski | VOS-30 | 7615 |

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| EXAMINER | |
|---|---|
| FETTEROLF, BRANDON J | |

| ART UNIT | PAPER NUMBER |
|---|---|
| 1642 | |

DATE MAILED: 04/06/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

| Office Action Summary | Application No. | Applicant(s) | |
|---|---|---|---|
| | 10/070,587 | WOJNOWSKI ET AL. | |
| | Examiner | Art Unit | |
| | Brandon J. Fetterolf, PhD | 1642 | |

*-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --*

**Period for Reply**

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

**Status**

1)☒ Responsive to communication(s) filed on *17 January 2006*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

**Disposition of Claims**

4)☒ Claim(s) *1,3-8,12,13,37,39 and 40* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1,3-8,12,13,37,39 and 40* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

**Application Papers**

9)☐ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *17 January 2006* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

**Priority under 35 U.S.C. § 119**

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

**Attachment(s)**

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

Wojnowski et al.

***Response to the Amendment***

The Amendment filed on 1/17/2006 in response to the previous Non-Final Office Action (7/15/2005) is acknowledged and has been entered.

Claims 1, 3-8, 12-13, 37 and 39-40 are currently pending and under consideration.

**The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office Action.**

**Rejections Maintained:**

***Claim Rejections - 35 USC § 112***

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Amended claim 1 is rejection and claims 3-8, 12-13, 37 and 39-40 remain rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claims 1, 3-8, 12-13, 37 and 39-40 remain rejected as vague and indefinite for reciting the term CYP3A4 as the sole means of identifying the claimed molecule. The use of laboratory designations only to identify a particular molecule renders the claims indefinite because different laboratories may use the same laboratory designations to define completely distinct molecules. The rejection can be obviated by amending the claims to specifically and uniquely identify CYP3A4, for example, by SEQ ID NO: and function of CYP3A4.

In response to this argument, Applicants contend that the subject matter of the amended claims is based on applicant's discovery of a phenotypic change associated with an amino acid substitution that results from a specific nucleotide change in a variant of the cytochrome P450 3A4 (CYP3A4) monooxygenase gene. Moreover, Applicants assert that the specification refers to the

sequence of CYP3A4 by GenBank accession number AF280107, wherein this accession number provides public access to the gene sequence of CYP3A4 and describes the gene as "Homo sapiens cytochrome P450 polypeptide 4 (CYP3A4)".

These arguments have been carefully considered, but are not found persuasive.

Regarding Applicants contention that the subject matter of the amended claims is based on applicant's discovery of a phenotypic change, the Examiner acknowledges that Applicants have discovered a phenotypic change in a variant of the cytochrome P450 3A4 monooxygenase gene. However, Applicant's arguments do not comply with 37 CFR 1.111(c) because they do not clearly point out how the amendments avoid such rejections. In response to Applicants assertion that the specification refers to the sequence of CYP3A4 by GenBank accession number CYP3A4 which provides public access to the gene sequence, the Examiner acknowledges that the specification refers to the sequence of CYP3A4 by GenBank accession number CYP3A4. Yet, the Examiner recognizes that different laboratories may use the same laboratory designations to define completely distinct molecules. As such, the use of the laboratory designation, CYP3A4, only to identify a particular molecule renders the claim indefinite.

***Claim Rejections - 35 USC § 102***

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (e) the invention was described in (1) an application for patent, published under section 122(b), by another filed in the United States before the invention by the applicant for patent or (2) a patent granted on an application for patent by another filed in the United States before the invention by the applicant for patent, except that an international application filed under the treaty defined in section 351(a) shall have the effects for purposes of this subsection of an application filed in the United States only if the international application designated the United States and was published under Article 21(2) of such treaty in the English language.

Claims 1, 4-7, 12-13, 37, and 39-40 remain rejected under 35 U.S.C. 102(e) as being anticipated by Larossa et al. (U.S. 6,025,131, 1996).

Larossa et al. teach a polynucleotide having, from nucleotides 134 to 144, the presently claimed polynucleotide of SEQ ID NO: 90 (Columns 33 and 34, see attached sequence comparison for sequence identifier 12). The Patent further teaches (column 4, lines 53-55, column 11, lines 2-14, and Figure 1) a vector comprising the polynucleotide further operatively linked to an expression control sequence which allows for the expression in prokaryotic or eukaryotic cells. Moreover,

Larossa et al. teach (page 4, lines 56-58) host cells with are genetically engineered with a vector comprising a polynucleotide operatively linked to an expression control sequence. Furthermore, the patent teaches (column 8, lines 60-67) a nucleic acid molecule which is complementary to the polynucleotide as the result of expression of the gene product, wherein the gene product is a protein. In addition, Larossa et al. (column 4, line 59 to column 5, line 2) provide a diagnostic composition comprising a probe useful for detecting chemical compounds, wherein said probe comprises a the polynucleotide operatively linked to a luminescent reporter gene complex. Lastly, the patent teaches a method for producing cells comprising genetically engineering cells with the polynucleotide (column 13, line 50 to column 14, line 34).

In response to this rejection, Applicants contend that claim 1 has been amended to recite an isolated polynucleotide encoding a variant CYP3A4 polypeptide or fragment thereof. As such, Applicants assert that the sequence referred to by the Examiner in Larossa is not a polynucleotide encoding a variant of CYP3A4 polypeptide or fragment thereof. Instead, the Larossa sequence is derived from a genomic segment isolated from E. coli and said to be a 205 base pair sequence that borders sulfometuron methyl (SM) responsive regulatory region in an unknown protein. See, e.g., column 4, lines 30-38. Thus, Applicants argue that the Larossa sequence cannot anticipate the subject matter of the amended claims.

These arguments have been carefully considered, but are not found persuasive.

Regarding Applicants assertion that the sequence disclosed by Larossa cannot anticipate the subject matter of the amended claims because the Larossa's polynucleotide is not a polynucleotide encoding a variant of a CYP3A4 polypeptide or fragment thereof, the Examiner acknowledges and agrees with Applicants arguments that Larossa's does not explicitly recite a polynucleotide which encodes a variant of a CYP3A4 polypeptide or fragment thereof. However, the Examiner recognizes that Larossa discloses a polynucleotide sequence which comprises, 100%, of the instantly claimed polynucleotide of SEQ ID NO: 90. Thus, although Larossa does not specifically teach that the polynucleotide encodes a variant of a CYP3A4 polypeptide or fragment thereof, the claims are drawn to the product *per se* and inherently, such a polynucleotide comprising SEQ ID NO: 90 would encode a CYP3A4 polypeptide. As such, the claimed polynucleotide appears to be the same as the prior art. The office does not have the facilities and resources to provide the factual evidence needed in order to establish that the product of the prior art does not possess the same material, structural

and functional characteristics of the claimed product. In the absence of evidence to the contrary, the burden is on the applicant to prove that the claimed product is different from those taught by the prior art and to establish patentable differences. See In re Best 562F.2d 1252, 195 USPQ 430 (CCPA 1977) and Ex parte Gray 10 USPQ 2d 1922 (PTO Bd. Pat. App. & Int. 1989).

Note: A sequence comparison of Larossa polynucleotide disclosed on Columns 33 and 34 compared to the currently claimed SEQ I DNO: 90 is provided below because Applicants did not receive the attachment with a sequence comparison accompanying the prior Office Action.

```
 Query Match             100.0%;  Score 11;  DB 3;  Length 205;
  Best Local Similarity   100.0%;  Pred. No. 1.1e+03;

Qy          1 TGAAATGCTCA 11  (SEQ ID NO: 90)
              ||||||||||
Db        134 TGAAATGCTCA 144  (Larossa's SEQ ID NO: 12)
```

**New Rejections upon reconsideration:**

***Priority***

Applicant's claim for foreign priority under 35 U.S.C. 119(a-d) is acknowledged. After reviewing the EPO application number 991 18 120.7 filed on 09/10/1999 for the disclosure of a polynucleotide comprising the nucleotides tgaaatgctca, e.g., SEQ ID NO: 90, specifically, a primer or probe consisting of about 15 to 50 nucleotides in length and comprising the nucleotide sequence of SEQ ID NO: 90, the Examiner has established a priority date of **September 1, 2000**, consistent with the filing date of the PCT application. If applicant disagrees with the rejection of claim 37 set forth in this office action based on examiner's establishment of a priority date of **September 1, 2000** for the instant claims in application serial number 10/070,587 applicant is invited to submit evidence pointing to the serial number, page and line where support can be found establishing an earlier priority date.

***Claim Rejections - 35 USC § 112***

The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 3-8, 12-13 and 39-40 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 3 recites the limitation "nucleotide deletion, addition and/or substitution" in claim 1. However, while there is sufficient antecedent basis in claim 1 for the limitation "substitution", there is insufficient antecedent basis for the limitation of an addition and/or deletion of a nucleotide in the claim.

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 1, 3-8, 12-13 and 39-40 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention because the specification does not provide evidence that the claimed biological materials are (1) known and readily available to the public; (2) reproducible from the written description.

It is apparent that the recited gene is required to practice the claimed invention, because they are specifically required in the claims. As required elements they must be known and readily available to the public or obtainable by a repeatable method set forth in the specification, or otherwise readily available to the public. If it is not so obtainable or available, the enablement requirements of 35 U.S.C. § 112, first paragraph, may be satisfied by a deposit of the gene listed in claim 1. See 37 CFR 1.802.

The specification does not provide a repeatable method for obtaining the nucleotide, and they do not appear to be readily available material. Deposit of the gene would satisfy the enablement requirements of 35 U.S.C. 112.

If a deposit is made under the terms of the Budapest Treaty, then an affidavit or declaration by applicants or someone associated with the patent owner who is in a position to make such assurances, or a statement by an attorney of record over his or her signature, stating that the deposit

has been made under the terms of the Budapest Treaty and that all restrictions imposed by the depositor on the availability to the public of the deposited material will be irrevocably removed upon the granting of a patent, would satisfy the deposit requirements. See 37 CFR 1.808.

If a deposit is not made under the terms of the Budapest Treaty, then an affidavit or declaration by applicants or someone associated with the patent owner who is in a position to make such assurances, or a statement by an attorney of record over his or her signature, stating that the deposit has been made at an acceptable depository and that the following criteria have been met:

(a) during the pendency of this application, access to the invention will be afforded to one determined by the Commissioner to be entitled thereto;

(b) all restrictions imposed by the depositor on the availability to the public of the deposited material will be irrevocably removed upon granting of the patent;

(c) the deposit will be maintained for a term of at least thirty (30) years and at least five (5) years after the most recent request for the furnishing of a sample of the deposited material;

(d) a viability statement in accordance with the provisions of 37 CFR 1.807; and

(e) the deposit will be replaced should it become necessary due to inviability, contamination or loss of capability to function in the manner described in the specification.

In addition, the identifying information set forth in 37 CFR 1.809(d) should be added to the specification. See 37 CFR 1.803 - 37 CFR 1.809 for additional explanation of these requirements.

***Claim Rejections - 35 USC § 102***

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (e) the invention was described in (1) an application for patent, published under section 122(b), by another filed in the United States before the invention by the applicant for patent or (2) a patent granted on an application for patent by another filed in the United States before the invention by the applicant for patent, except that an international application filed under the treaty defined in section 351(a) shall have the effects for purposes of this subsection of an application filed in the United States only if the international application designated the United States and was published under Article 21(2) of such treaty in the English language.

Claim 37 is rejected under 35 U.S.C. 102(e) as being anticipated by Mittman et al. (US 6,821,724, 1999).

Mittman et al. teach a nucleic acid probe consisting of 25 nucleotides in length and comprising the patentably claimed nucleotide sequence of SEQ ID NO: 90 or a complementary sequence as shown below.

```
US-6,821,724 (SEQ ID NO:71432)

  Query Match             100.0%;  Score 11;  DB 4;  Length 25;
  Best Local Similarity   100.0%;  Pred. No. 8.1e+02;
  Matches   11;
Qy          1 TGAAATGCTCA 11 (SEQ ID NO: 90)
              ||||||||||
Db         12 TGAAATGCTCA 2 (SEQ ID NO: 71432)
```

Therefore, No claim is allowed.

**All other rejections and/or objections are withdrawn in view of applicant's amendments and arguments there to.**

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Brandon J. Fetterolf, PhD whose telephone number is (571)-272-2919. The examiner can normally be reached on Monday through Friday from 7:30 to 4:30.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Jeff Siew can be reached on 571-272-0787. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Brandon J Fetterolf, PhD
Examiner
Art Unit 1642

BF

JEFFREY SIEW
SUPERVISORY PATENT EXAMINER